MEDICAL STAFF CONFERENCE

Autonomic Insufficiency

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California, San Francisco. Taken from transcriptions, they are prepared by Drs. Sydney E. Salmon and Robert W. Schrier, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. SMITH:* The topic for presentation this morning is autonomic insufficiency. Dr. Pate Thomson will present in sequence three patients for consideration.

DR. THOMSON:† I am going to break with the usual format of Medical Grand Rounds to discuss with you some of the cardiovascular reflex testing we do in patients with autonomic insufficiency. I will present the patients and the results of their tests, so that the studies will be more meaningful.

Pathophysiology

I would like to give you some background as to how the concept of neurovascular control of the cardiovascular system developed. Although in the 19th century a number of people had observed that syncope may be related to upright posture, it was not until 1895 that Leonard Hill,[1,2] a British physiologist, reported on blood pressure response to changes in position in many species of quadriped and biped animals. He concluded that man and other biped animals have a system which combats the hydrostatic effects of gravity on the circulating blood. This process, which he thought to be mediated through splanchnic vasoconstriction, is less well developed in quadriped animals. He postulated that abnormalities in the system could exist in man. However, it was not until 1925 that Bradbury and Eggleston[3] reported the first clinical series of three patients with postural hypotension including the features shown in Table 1. Several factors about this description are noteworthy. The first is that it is a remarkably complete list in light of our present experience with the disease or syndrome. The second factor is that paralysis of the autonomic nervous system produces many effects beyond the orthostatic hypotension. For example, the ability to dissipate heat is impaired, metabolic rate is slowed, renal function is posturally dependent, sexual function is compromised (all males are impotent), the hematological system is involved, and gastrointestinal disturbances occur as well.

The report by Bradbury and Eggleston[3] set the stage for what has come to be well recognized as a clinical syndrome. It has been of interest in this institution since 1960, when Dr. McIlroy* and Dr. Brown† began to study the cardiovascular reflexes and various other aspects of these cases. More recently, Dr. Vetter, who will present one of the cases today, Dr. Ehrlich‡ and I have been involved in these studies. We are at present following 24 patients who have undergone a rather complete study of cardiovascular reflexes. This experience has emphasized three factors. The first factor is diversity of pres-

*Lloyd H. Smith, Jr., M.D., Professor and Chairman, Department of Medicine.
†Pate D. Thomson, M.D., Instructor in Medicine.

*Malcolm McIlroy, M.D., Professor of Medicine.
†Ellen Brown, M.D., Professor of Medicine.
‡Ira Ehrlich, M.D., Former trainee in cardiology.

TABLE 1.—*Clinical Features of Bradbury and Eggleston (1925)*[3]

Orthostatic hypotension
Syncope
Fixed heart rate
Heat intolerance
Anhidrosis
Low basal metabolic rate
Slight and indefinite signs of neurological disease
Nocturnal polyuria
Impotence
Youthful appearance
Pallor
Anemia
Chronic diarrhea

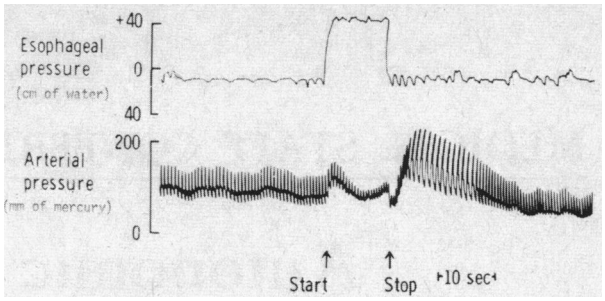

Figure 1.—A normal blood pressure response to Valsalva's maneuver in a young patient.

entation of the syndrome, which we will illustrate with three cases. The second factor is the variation of cardiovascular reflex abnormalities and the inability to relate a given pattern of abnormality to any specific etiological process. The third factor is the therapeutic response which, contrary to widely held medical opinion, may be dramatic and rewarding when approached in a physiological manner.

What is the basic clinical approach? Given circumstances in which there is some reason to suspect this diagnosis (such as fainting or other orthostatic symptoms), the first approach is to exclude the diagnosis of autonomic insufficiency. In our experience the most sensitive test is simply the measurement of an orthostatic fall in blood pressure. If there is no fall in mean blood pressure after the patient has been standing for two to three minutes and if there is no blood pressure fall after brief bedside exercise, then (in my opinion based on the experience of our studies) the patient does not have a disturbance in the neurovascular control of the cardiovascular system. That is, he does not have autonomic insufficiency. If a fall in blood pressure in these circumstances is demonstrated, there are a number of possible causes independent of autonomic dysfunction. If orthostatic hypotension is demonstrated, I believe it is incumbent upon the physician to define the abnormality.

Measurements of serum potassium, blood volume and, in selected cases, adrenal function are useful. However, there is a more direct approach by which one may quite confidently identify the syndrome. The first and most important test is direct arterial blood pressure recording of the Valsalva's response (Figure 1). The patient is asked to blow into a manometric device to generate a pressure of 40 cm of water and to maintain that pressure for 10 to 15 seconds, while the blood pressure response is recorded. With the first effort there is a transient rise in blood pressure for a few beats. This rise in pressure probably results from squeezing blood out of the lungs into the left ventricle and from the augmentation of ventricular ejection secondary to the imposition of a transpulmonary pressure of 40 cm of water. As this straining maneuver is maintained, inflow to the right side of the heart and subsequent inflow to the left side of the heart is impeded. As a result cardiac output and pulse pressure fall, stimulating baroreceptors to initiate reflex vasoconstriction, which can usually be recognized by a plateau or recovery of blood pressure during the late phase of the straining maneuver. Then, with release of straining, there is a sudden increase in venous return, and the ventricle ejects a large volume of blood which meets a constricted peripheral vascular bed. When this occurs, there is overshoot of blood pressure. The baroreceptors detect the hypertension and reflexly dampen the response, slowing heart rate and initiating vasodilatation. Over a short period the blood pressure returns to normal. When an individual is in the 50 to 70 age group, the amount of overshoot is reduced. The tracing shown is from a young person.

Figure 2 shows the Valsalva's response of the first patient (Case 1) that we will present. During the straining maneuver the first few beats of the response are normal; then blood pressure falls rather rapidly and abruptly during the strain. Notice that there is no plateau of pressure during the strain. This absence of plateau is also characteristic of patients with autonomic insufficiency. When the patient releases the strain, the most striking abnormality is exhibited. There is no overshoot in the systolic or diastolic blood pressure; instead there is a gradual return

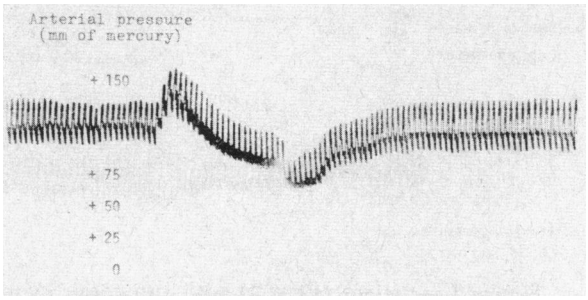

Figure 2.—Blood pressure response to Valsalva's maneuver in a young patient (Case 1) with autonomic insufficiency.

toward normal. Also note that this patient does have an acceleration of heart rate during the strain. This acceleration has been a confusing point clinically to those who evaluate patients demonstrating autonomic insufficiency. The heart rate need not be fixed in this syndrome even though the original publications described it as fixed. Only 40 percent of our patients have fixed heart rates.

Figure 3 is a diagrammatic representation of the reflex pathways under consideration. The Valsalva's response causes changes in blood pressure which are detected by the baroreceptor mechanisms. The reflex arc includes the baroreceptor and its afferent nerve (E), a central integration of this process (A), subsequent sympathetic outflow (B), and then an end organ response which we measure (G). Valsalva's maneuver tests the whole reflex pathway. If the disease process causing orthostatic hypotension is limited to the baroreceptor or its afferent nerve, it may be demonstrated by eliciting a pressor response to another stimulus to the sympathetic nervous system, such as the painful cold pressor stimulus (D—→ A—→ B—→ G), or an emotional stress such as the performance of rapid mental arithmetic (A—→ B—→ G). The next point in the pathway that may be tested is the nerve ending. If nerve endings exist and if they are able to release norepinephrine, we expect a pressor response to tyramine which normally releases norepinephrine from nerve endings (B—→ G). Finally, to exclude a primary abnormality of vascular smooth muscle responsiveness, norepinephirne is infused. A rise in blood pressure excludes alpha blockade or a primary defect in end organ responsiveness (G).

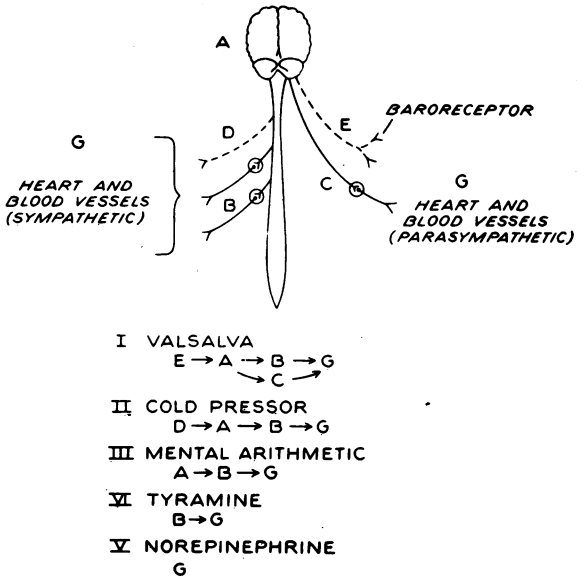

Figure 3.—A diagrammatic representation of reflex pathways tested by the several maneuvers listed.

There are certain conditions which will influence end organ responsiveness. Hypokalemia,[4,5] adrenal insufficiency,[6] and systemic amyloidosis[4] have been shown to exhibit the phenomenon of end organ insensitivity and yield an absence or reduction of pressor response to infused norepinephrine. In our experience, however, a more common cause of noreprinephrine insensitivity is the use of outdated, inactive norepinephrine.

Case Presentations

With that background I will present the three patients who serve to illustrate the diversity of the syndrome as well as the typical clinical features and the response to therapy. The first patient (Case 1) is a 26-year-old woman whose symptoms of diabetes began in January 1969. Insulin therapy was not begun until July 1969, by which time her body weight had decreased 25 pounds. A painful and disabling peripheral neuropathy began in July 1969 and is still present. Control of diabetes during this time was never adequate. Orthostatic hypotension was first noted on admission to this hospital for diagnosis of neuropathy. On physical examination orthostatic hypotension with a variable heart rate was noted. The patient was cachectic (weight 75 pounds). She had stocking-glove hypesthesia and hypalgesia as well as subjective painful paresthesia of the hands and feet. Persistent

hyponatremia and hypo-osmolarity were present and are currently under investigation at the San Francisco General Hospital. Laboratory tests revealed a reduced erythrocyte volume, a condition noted in a majority of our patients. Serum potassium, plasma and urinary steroids were within normal limits.

The Valsalva response (Figure 2) lacks a plateau during the strain phase and lacks a blood pressure overshoot. With this stimulus to the baroreceptors, the patient is unable to initiate any peripheral vasoconstriction, but she is able to increase heart rate. Blood pressure rose in response to cold pressor and mental arithmetic stresses. This rise indicates she has an effective efferent sympathetic pathway to the blood vessels that is not stimulated by baroreceptors. Lowering the blood pressure with amyl nitrite and upright posture increased the heart rate and further documented that she had normal baroreceptor heart rate responses. Raising the blood pressure with angiotensin resulted in a slowing of the heart rate, thereby testing the vagal side of the baroreceptor reflexes and showing the response to be normal. The patient responded normally to norepinephrine and tyramine infusions. Our interpretation is that she has a central nervous system defect which prevents integration of baroreceptor stimuli with the sympathetic outflow to the peripheral vascular bed.

This case then illustrates that the syndrome may afflict young persons. In patients less than 40 years of age who have acquired the disorder, autonomic insufficiency is always accompanied by overt diabetes mellitus and other signs of neuropathy. The case also illustrates an unusual central neurological lesion which appears to be responsible for the orthostatic hypotension.

The second patient (Case 2) is a 52-year-old man with dry skin and a youthful appearance. He noted impotence at age 47, postural giddiness at age 48, and syncope at age 50. He has noted decreased sweating and increasing lightheadedness which is worse in the morning and aggravated by exercise and hot weather. On physical examination, orthostatic hypotension with a variable heart rate are noted. He has no neurological abnormalities. Interestingly, the blood glucose level is high at one hour, with hypoglycemia occurring after two hours. Reactive hypoglycemia is present in many of the patients that we test. Since epinephrine release is known to

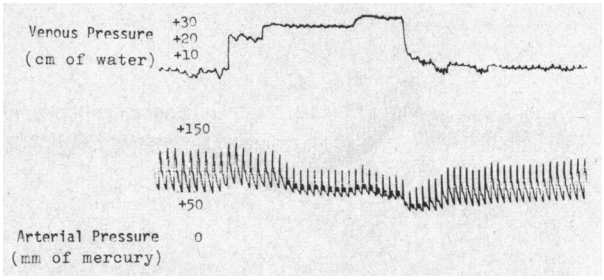

Figure 4.—Patient (Case 2) with autonomic insufficiency did not have overshoot of systolic and diastolic blood pressure in response to Valsalva's maneuver.

be defective in these patients, presumably one of their major defenses against hypoglycemia is lost, thus accounting for this phenomenon.

Figure 4 demonstrates his Valsalva's response. Note that the patient (Case 2) has a step-wise decrease in blood pressure during the strain which mirrors a step-wise increase in intrathoracic pressure, and he does not have an overshoot of the systolic and diastolic pressure. In addition his blood pressure does not rise in response to cold pressor and mental arithmetic stresses. Lowering the blood pressure with amyl nitrite and upright posture results in an increase in heart rate whereas raising blood pressure with angiotensin results in a slowing of heart rate, which indicates that the baroreceptor function as it relates to the heart rate control is normal. The patient has exaggerated pressor responses to norepinephrine, tyramine, and angiotensin.

We interpret this pattern to be most compatible with peripheral neuropathy involving the autonomic nervous system. No matter what afferent stimulus is used, we are unable to effect a vasoconstriction response. However, if we stimulate the periphery with pressors the patient has an inordinate response suggesting denervation hypersensitivity.

The patient is here for presentation this morning. (Patient enters.)

DR. THOMSON (to patient): Will you describe for the audience what therapeutic program you are following?

PATIENT: I am taking 0.1 mg of fludrocortisone acetate (Florinef®) daily. I wear knee-length elastic hose and elastic briefs, and I have the head of my bed elevated approximately 5 inches.

DR. THOMSON: How would you describe the effect of your treatment?

PATIENT: I am tremendously improved and barely notice any symptoms in the morning or after strenuous exercise such as climbing a hill or walking upstairs. For example, when I came here this morning I had to park at the bottom of the hill. Most of you know what a healthy climb it is from three blocks down, and this morning that did not affect me even slightly. I was surprised at the improvement.

DR. THOMSON: How would you have done before treatment?

PATIENT: Before treatment I would have sat down at least two times if I had had to climb a hill like that, and when I arrived in the lobby I probably would have stretched out.

DR. THOMSON: One of your symptoms before elevating the head of the bed was to get up once or twice a night to go to the bathroom. Do you notice that is any different now?

PATIENT: Yes, that has greatly improved. I seldom have to get up at night now to urinate unless I am away on vacation or business where I do not have a bed with the head elevated. Then I notice that it comes back so that the frequency may be as much as two or three times a night.

DR. THOMSON: When you are having nighttime urinary frequency, do you notice an increase in lightheadedness?

PATIENT: Very definitely.

DR. THOMSON (to audience): The patient went on a vacation and in motels was sleeping flat without elevation of his head, and during that period he had nocturia several times and return of his early morning symptoms. I want to bring that up as a therapeutic point later.

PHYSICIAN IN AUDIENCE: Do you have ankle swelling now?

PATIENT: No.

PHYSICIAN IN AUDIENCE: Does your weight differ when you take Florinef®?

PATIENT: I have not noticed a variation of more than two pounds. I might add that I have been particularly careful of my diet. When I went on Florinef® I was advised to watch my weight.

DR. THOMSON: Thank you very much for coming in. (Patient leaves.)

This patient illustrates many of the typical features of autonomic insufficiency—impotence, decreased sweating, nocturnal polyuria, aggravation of symptoms in the early morning and by exercise and hot weather. The patient's response to treatment has been gratifying but not unusual. Elevation of the head of the bed reduces the nocturnal diuresis which most of these patients have. Eliminating this diuresis improves the early morning hypotension and illustrates the extreme sensitivity of these patients to minor changes in blood volume. On Florinef® this patient's supine blood pressure is 150/100 mm of mercury, and elevating the head of the bed protects him from prolonged hypertension.

Dr. Vetter will present the third patient.

DR. VETTER:* The third patient (Case 3), evaluated at the United States Public Health Service Hospital, is an older man whose initial symptoms were those of carotid sinus hypersensitivity. He is presented to expand what is at present considered the spectrum of autonomic insufficiency. We believe the findings indicate selective sympathetic cardiac denervation. The patient is a 74-year-old, retired Coast Guard officer who was readmitted in September 1969 to the USPHS Hospital in San Francisco because of a four-hour episode of severe substernal pain which was unrelieved by nitroglycerine therapy.

The patient had been admitted to hospital one year previously for lightheadedness, especially after arising rapidly, during physical straining and following exercise. (For example, after pushing a loaded supermarket cart, the patient could prevent dizziness caused by standing still in the checkout line only by walking in place.) Two episodes of syncope had occurred, both associated with hyperextension of the neck, immediately after standing. He had no warning before the attacks. He regained consciousness immediately upon falling to the floor and he had no residual symptoms. The patient had had angina pectoris for ten years and it had responded poorly to nitroglycerine therapy.

On examination during the first hospital admission, the heart rate was 50 to 55 per minute. Mild orthostatic hypotension was noted and there was a bruit over the right carotid artery. Pressure on the right carotid sinus (Figure 5), produced 6 seconds of sinus arrest with asystole followed by gradual resumption of the previous sinus rate. An aortic arch angiogram showed partial occlusion of the right internal carotid artery. This was not thought to account for the symptoms. Atropine therapy for carotid sinus

*William R. Vetter, M.D., Research Associate in Medicine, USPHS Hospital, San Francisco, and Clinical Instructor in Medicine, University of California, San Francisco.

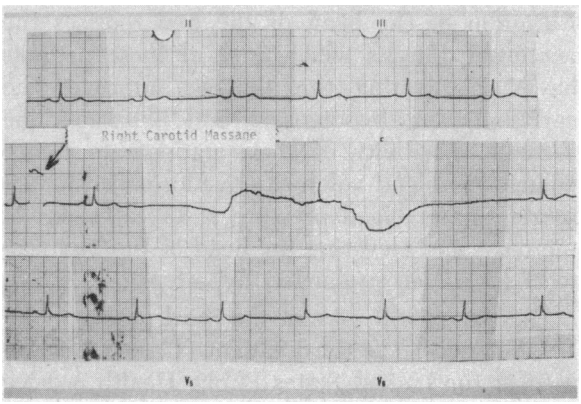

Figure 5.—Right carotid sinus massage, at arrow, produced 6 seconds of sinus arrest with asystole (Case 3).

hypersensitivity was begun. The patient was advised against wearing tight collars. No further syncopal episodes occurred, but anginal attacks unrelieved by nitroglycerine therapy became more frequent.

At the time of the second hospital admission the heart rate was 50 beats per minute and the blood pressure 150/80 mm recumbent and 130/70 mm standing. The electrocardiogram and serum enzymes remained within normal limits. Serum electrolytes, fasting blood sugar and indices of renal function were also within normal limits. Blood volume, determined by ^{131}I albumin dilution, was strikingly increased to 10 liters.

Because of the slow heart rate and history of dizziness after exercise, studies of autonomic cardiovascular reflexes were performed (Table 2) by employing direct arterial pressure measurements. The response to Valsalva's maneuver was abnormal, as no overshoot of pressure followed hypotension, and the rate remained fixed despite hypotension. Hypotension without increase in rate occurred at one minute of 70° upright tilting. Despite 20 to 40 mm of mercury rise in arterial pressure during cold pressor and mental arithmetic tests, the heart rate was unchanged. Amyl nitrite inhalation caused pronounced hypotension from the control values of 156/60 to 83/30, but no increase in rate occurred. A gradual rise in rate did occur during supine bicycle exercise.

With a temporary, transvenous demand pacemaker in place, right carotid sinus massage was performed. Sinus arrest occurred and the temporary pacemaker responded. Mild hypotension,

TABLE 2.—*Cardiovascular Reflex Studies in Patient (Case 3) with Autonomic Insufficiency*

	Pulse (beat/min)	Blood Pressure (mm Hg)
Valsalva		
Baseline	52	150/55
Minimum	52	80/40
Overshoot	55	140/56
Mental Arithmetic		
Control	52	160/60
Maximum	52	202/80
Cold Pressor		
Control	52	160/60
Maximum	52	202/80
70° Tilt		
Control	52	160/60
1 minute 30 seconds	52	125/48
Supine Bicycle Exercise		
Control	52	160/60
4 minutes 25 watts	60	180/60
2 minutes 50 watts	70	200/65
Amyl Nitrite Inhalation		
Control	50	150/60
Minimum	54	86/30
Angiotensin (0.25 micrograms IV)		
Control	46	160/58
Maximum	46	180/70
Atropine (0.8 micrograms IV)		
Control	46	148/52
Maximum	56	160/80

a drop from 140/60 to 120/50 mm, was noted during carotid massage, but this did not produce symptoms. Small doses of angiotensin and norepinephrine increased arterial pressure but did not slow the heart rate. Isoproterenol increased the sinus rate. A permanent, transvenous demand pacemaker was implanted to avoid syncopal episodes, and the patient has done well since discharge from hospital.

We conclude that this patient's illness, initially diagnosed as carotid sinus hypersensitivity, was the result of autonomic insufficiency with predominantly sympathetic cardiac denervation. Parasympathetic effects on heart rate evoked by carotid sinus massage were unopposed by the compensatory sympathetic cardioaccelerator mechanism. The carotid sinus was not hypersensitive to physiological stimuli, as there was no slowing of heart rate in response to increased blood pressure produced by angiotensin. Apparent carotid sinus "hypersensitivity" was the result of loss of the sympathetic cardioaccelerator function which prevents prolonged asystole in normal persons subjected to carotid massage.

Similarly, slow resting rate reflected unopposed parasympathetic effects.

DR. THOMSON: We have tried to present a diverse series to stimulate your interest in this entity. We have also illustrated how we study these patients.

Therapy

As far as therapy is concerned, the key to management of these patients, in my opinion, is an appreciation of the important fact that blood pressure is a sensitive index of blood volume in patients who do not have sympathetic innervation. Minor manipulations of blood volume on the positive side produce dramatic responses in blood pressure, and this manipulation is employed therapeutically. On the other hand, with reduction of blood volume resulting from minor blood loss or gastrointestinal illness (accompanied by either vomiting, diarrhea or both) may produce profound hypotension. The major risk to life in these patients relates to this phenomenon. The physician and patient must work to protect the blood volume. Both must appreciate that if the patient has diarrhea, vomiting, operation, or other trauma, every attention should be directed to control of the blood volume.

The therapeutic maneuvers that we generally use in these patients involve fludrocortisone acetate (Florinef®), 0.1 to 0.2 mg per day. This medication expands blood volume and dramatically supports blood pressure in most patients. Elevation of the head of the bed with 6-inch blocks produces many benefits, as discussed previously. We employ these maneuvers with almost every patient.

In addition to Florinef®, we frequently use elastic garments (tailored by the Jobst Service Center) which provide elastic support to above the waist. These garments are rather difficult to put on and a patient may be reluctant to wear them, but in severe cases they are necessary. Smaller elastic garments, such as elastic hose, are often helpful and better tolerated by the patient.

A great effort should be made toward educating patient and family as to the nature of the illness. They must know how to cope with fainting spells, how to avoid certain situations that aggravate hypotension (such as heat, exercise, and prolonged standing). They must understand the need for medical supervision during gastrointestinal illnesses. Environmental adjustments, such as an air conditioner for the car or home, may be quite helpful.

Finally, I will comment about ephedrine, a commonly used drug in the treatment of these patients. It generally has given disappointing results because it produces a rapidly developing tachyphylaxis. Since all patients become unresponsive to it after several days of treatment, we instruct them to use 50 mg four times daily during periods when symptoms are severe, but to limit the course to three days because the drug is ineffective beyond that time. Although this program has pharmacological rationale, I am not certain that it produces beneficial results.

Recently Sellars[7] published a report of a case of refractory orthostatic hypotension treated by combining a monamine oxidase inhibitor with hydroxyamphetamine, which acts by the same mechanism as ephedrine and releases norepinephrine from the nerve endings. Monamine oxidase inhibitors are thought to permit accumulation of norepinephrine stores; for this reason Sellars postulated that the tachyphylaxis does not develop. There is another mechanism which may be operating in this case. Monamine oxidase inhibitors inhibit the metabolism of hydroxyamphetamine, and this may be an important factor in the prolonged response that he observed.

DR. SMITH: I would like to thank Dr. Thomson and Dr. Vetter for a very excellent presentation. We have in the audience a number of people who have made contributions in the study of this disease. Dr. Brown, will you comment about this problem or these patients?

DR. BROWN: I think this has been a profitable presentation, primarily from the practical point of view. There are some exciting things that have been revealed by studying more carefully a variety of patients. I certainly agree that those patients presented today have an enormous diversity of causes of orthostatic hypotension as well as a diversity of manifestations of autonomic insufficiency. Some of these patients are unable to regulate either cardiac rate, stroke volume, or muscular performance. Some of them are relatively unable to regulate their resistance blood vessels. It is well known that these vessels cannot constrict or may have faults in constriction in response to thermal stress. Similarly, the patients may have defective sweating, which in my

experience is usually quite patchy. I am not sure that any one has demonstrated actual deficiency of temperature regulation. Heat imposes an additional stress.

I think we came across the blood volume phenomenon completely by accident. It is quite impressive. In our patient population 50 percent or more with autonomic insufficiency have major disturbances in the blood volume regulation. This involves both the sodium regulation and also the erythropoietic response. Theoretically, since the patients are pooling blood peripherally when they are upright, they ought to be making extra blood if they have an adequate physiological response. It should be similar to hemorrhagic response. In fact, they have a gross deficiency of red cell mass if you compute it in relation to what you would predict to be normal. The deficiency is as much as 20 to 30 percent of the red cell mass, and this is a clue to the diagnosis. There is still a large gap in information about how the erythropoietic response is handled. This response implies some autonomic involvement in volume regulation for cell mass as well as for sodium and water. The safe way to test patients at the bedside is to measure the blood pressure response in the recumbent subject after exercise.

DR. SMITH: Another member of the audience whose work has been widely quoted this morning is Malcolm McIlroy. Do you wish to comment, Dr. McIlroy?

DR. MCILROY: This group of diseases is really a wastebasket at the moment, and we do not understand completely this disease syndrome. There are only a few postmortem examinations cited in the literature, and the pathological-anatomical extent of the disease of the nervous system is relatively unknown. What is needed is serial sectioning of the nervous system performed by a neuropathologist immediately after the patient has died.

DR. HAVEL:* Dr. Thomson mentioned that the diabetic patient got better with treatment, and I would like to mention that I do not believe that this is necessarily cause-and-effect. In fact, we have observed severe orthostatic hypotension develop in well-controlled diabetes.

*Richard J. Havel, M.D., Professor of Medicine.

GENERIC AND TRADE NAMES OF DRUGS

Fludrocortisone acetate—Florinef®

REFERENCES

1. Hill L: The influence of the force of gravity on the circulation. J. Physiol 18: 15, 1895
2. Hill L, Bernard H: The influence of the force of gravity on the circulation (Part II). J Physiol 21: 323, 1897
3. Bradbury S, Eggleston C: Postural hypotension: Report of three cases. Amer Heart J 1: 73, 1925
4. Friedman M, Freed, SC, Rosenman RH: Effect of potassium administration on 1) peripheral vascular reactivity and 2) blood pressure of the potassium depleted rat. Circulation 5: 415, 1952
5. Wagner HN Jr: Orthostatic hypotension. Johns Hopkins Med J 105: 322, 1959.
6. Freed SC, Rosenman RH, St. George S, *et al*: Effect of cortisone and ACTH on blood pressure of hypotensive, potassium deficient rats. Circ Res 2: 41, 1954
7. Sellars RH: Idiopathic orthostatic hypotension. Amer J Cardiol 23: 838, 1969

A HALO MEANS SPINAL FLUID

"When assessing an apparently traumatic spinal fluid tap, allow a drop of the red fluid coming out of the needle to drop on either paper or the bed sheet, and then inspect the edge of the spreading impregnation. If the edge is sharply red with no border of wetness beyond it, then it is pure blood. If there is spinal fluid on it, there will be a noncolored margin of a millimeter or more extending beyond the advancing margin of the red discoloration."

—N. JOEL EHRENKRANZ, M.D., Miami

Extracted from *Audio-Digest General Practice*, Vol. 17, No. 24, in the Audio-Digest Foundation's subscription series of tape-recorded programs.